REMARKS

This Amendment and Response are submitted in response to a non-final Office Action mailed on November 1, 2004.

Claims 1-11, 19, 21, 27, 29, 35, and 37 have been canceled without prejudice or admission. Claim 12 has been amended to (1) include the limitations of cancelled claim 1 and (2) limit the claim to an isolated nucleic acid encoding a truncated α-crystallin protein that forms an aggregate having a mass of approximately 60,000 Daltons. Support for this amendment can be found on page 45, lines 14-19 and on page 13, lines 12-19 of the specification. Claim 13 has been amended to include the limitations of cancelled claim 4, as requested by the Examiner. Claims 14-17 have been amended to define precisely the term "stringent conditions." Support for these amendments can be found on page 24, lines 8-11 of the specification. Claims 14 and 15 have also been amended to depend on claims 12 and 13, respectively, thereby removing dependency from cancelled claims. Additionally, claims 16 and 17 have been amended to remove a reference to a figure which redundant in light of the claim reciting SEQ ID NO:2.

Claims 18, 26, and 34 have been amended to include (1) the limitations of cancelled claims 19 and 21, 27 and 29, and 35 and 37, respectively; and (2) the limitation of a truncated α-crystallin protein that forms an aggregates having a mass of approximately 60,000 Daltons. Support for these amendments can be found on page 45, lines 14-19 and on page 13, lines 12-19 of the specification. Claims 20, 22, 24, 25, 28, 30, 32, 36, and 38-40 have been amended to make them dependent from pending, rather than canceled, claims.

New claims 42-47 are identical to claims 12, 14, 16, 18, 26, and 34 except that these claims are limited to nucleic acids that encode for a "truncated polypeptide that retains the ability of the wild-type protein to prevent protein aggregation," instead of a truncated polypeptide that forms an aggregate having a mass of approximately 60,000 Daltons. Support for these amendments can be found on page 45, lines 20-22 of the specification and in Figure 8.

New dependent claims 48 and 49 further limit claim 12. Support for these new claims can be found on, for example, page 9, lines 10-13 of the specification.

Thus, with entry of this Amendment, claims 1-11, 19, 21, 27, 29, 35, and 37 are cancelled and claims 12-18, 20, 22-26, 28, 30-34, 36, and 38-49 are pending (of which claims 18, 20, 22-26, 28, 30-34, 36, and 38-41 are withdrawn).

Election/Restrictions

The Examiner has acknowledged the Applicant's election of Group II (claims 12-17 directed to isolated nucleic acids encoding truncated α-crystallin polypeptides). Claims 18, 20, 22-26, 28, 30-34, 36, and 38-41 of Group III process claims have been withdrawn from consideration. However, as acknowledged by the Examiner in paragraph 6 of the Restriction Requirement mailed June 17, 2004, should Group II product claims be found allowable, withdrawn Group III process claims which depend from or otherwise include all the limitations of the allowable product claims will be rejoined as a matter of right according to MPEP §821.04.

Applicants would like to respectfully note to the Examiner that claims 18, 26, and 34 have been amended to be consistent with the amendments made to the elected group (claims 12-17), and thus contain all of the limitations of the elected group. Applicant respectfully ask the Examiner to rejoin these non-elected claims and any claims dependent from these claims, if any elected claim is found allowable.

Additionally, applicants respectfully request the Examiner to consider new claims 42-44, 48, and 49, since they are directed to the same invention as the elected group, isolated nucleic acids encoding truncated α-crystallin polypeptides. New claims 45-47 are directed to non-elected group III, however they include all of the limitations of the elected group. Applicants respectfully ask the Examiner also to rejoin these non-elected claims, if any elected claim is found allowable.

Information Disclosure Statement

Enclosed with this Amendment is the Smulder *et al.* (*Int. J. Biol. Macromol.*, 22: 187-96 (1998)) reference (attached as Exhibit 1) that was not received by the PTO, but was listed on the IDS filed on June 4, 2004 as cite number "CE." Acknowledgement of consideration of this reference is respectfully requested.

Claim Rejection 35 USC §112

Claims 12-17 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the invention. Specifically, claims 12-15 have been rejected for being dependent on withdrawn claims 1 and 4. In addition, claims 14-17 have been rejected for the lack of clarity of the term "stringent conditions."

Claims 12-17 have been amended to render this rejection moot. Specifically, claims 12-15 have been amended to no longer depend on withdrawn claims. Furthermore, claims 14-17 have been amended to define stringent conditions by listing specific incubation conditions. Accordingly, Applicants respectfully request withdrawal of these rejections.

Claim Rejection 35 USC §102

Claims 12, 14, and 16 have been rejected under 35 U.S.C. 102(b) as being anticipated by Kamei *et al.* (*Biochemical and Biophysical Research Communications*, 231: 373-378 (1997); "Kamei"). According to the Examiner, Kamei discloses the isolation and sequencing of N-terminal human α-crystallin polypeptides from human lens tissue. The Examiner further cites Kamei as disclosing α-crystallin polypeptides that have from 1 to 6 amino acids truncated from the N-termini of αA- or αB-crystallin polypeptides. The Examiner argues that the polypeptides are inherently encoded by nucleic acid sequences.

Applicants respectfully traverse this rejection. Applicants would like to point out to Examiner that claims 12, 14, and 16 are directed to isolated nucleic acids. Isolated nucleic acids are not inherent properties of the polypeptides. According to MPEP §2112(IV), "'In relying upon the

theory of inherency, the Examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applies prior art.'" *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. Appl. & Inter. 1990) (emphasis in original). Isolated nucleic acids do not necessarily flow from the prior art peptides because nucleic acids and peptides are separate compositions of matter. It is well known to those of skill in the art that possession of an isolated polypeptide does not mean that one has possession of the corresponding nucleic acid, much less the isolated nucleic acid. In view of these points, Kamei does not anticipate the current invention. Accordingly, withdrawal of this rejection is respectfully requested.

Claim Rejection 35 USC §103(a)

Claims 12, 14, and 16 have also been rejected as obvious over Andley *et al.* (*Journal of Biological Chemistry*, 271: 31973-31980 (1996); "Andley") in view of Kamei. Andley allegedly discloses the cloning, expression, aggregation behavior, and chaperone-like activity of human αA-crystallin and mutants of human αA-crystallin. The Examiner alleges that the nucleic acid sequence disclosed by Andley encoding a human αA-crystallin protein describes the nucleic acid sequence encoding the truncated αA-crystallin protein disclosed in Kamei.

Applicants have amended the claims to render this rejection moot. Elected claims 12, 14, 16 and non-elected claims 18, 26, and 34 have been amended to limit the claims to truncated α-crystallin proteins that form aggregates having a mass of approximately 60,000 Daltons.

At a minimum, Andley teaches that C-terminal truncations or amino acid point mutations (W9F) result in larger or in the same size aggregates, respectively, compared to 540 kDa wild-type aggregates (see pg. 31977 of Andley). Andley does not suggest or teach that truncations could result in smaller aggregates. Applying the teaching of Andley to Kamei would lead a person skilled in the art to conclude that the truncated proteins observed in Kamei would produce larger or the same size aggregates as wild-type aggregates. Taken alone, Kamei does not teach or suggest that the removal of N-terminal amino acids would reduce aggregation. Thus, neither Andley nor Kamei,

taken separately or combined, teach or suggest that truncated α-crystallin proteins result in smaller aggregates than wild-type α-crystallin proteins. Accordingly, applicants respectfully request withdrawal of this rejection.

Applicants have also added new claims 42-47, which are limited to truncated polypeptides that retain the ability of the wild-type protein to prevent aggregation. Claims 42-47 are neither anticipated nor obvious in light of Andley and Kamei. Andley teaches that C-terminal truncations would reduce the chaperonin-like properties of wild-type α-crystallin and discloses only that a minor amino acid point mutation (W9F) preserves the chaperonin-like properties of the wild-type protein (see pg 31978-31980 of Andley). Kamei suggests that omission of N-terminal amino acids would reduce the chaperonin properties of α-crystallin (pg. 373, introductory paragraph of Kamei). Hence, Kamei teaches away from the claimed invention that shows N-terminal truncations preserve the chaperonin activity of the wild-type protein. Thus, either reference, taken individually or together, does not suggest or teach that truncations would preserve the chaperonin-like properties of the wild-type protein. Accordingly, allowance of new claims 42-47 is respectfully requested.

Conclusion

In view of the above amendments and remarks, applicant believes the pending application is in condition for allowance. If there are any other issues remaining which the Examiner believes could be resolved through either a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at the telephone number indicated below.

Dated: April 1, 2005

Respectfully submitted,

By Heather Morehouse Ettinger

Heather Morehouse Ettinger, Ph.D.
Registration No.: 51,658
DARBY & DARBY P.C.
P.O. Box 5257
New York, New York 10150-5257
(212) 527-7700
(212) 527-7701 (Fax)
Attorneys/Agents For Applicant